

The effects of hydroxyapatite nano-coating  
implants on healing of surgically created  
circumferential gap in dogs

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# The effects of hydroxyapatite nano-coating implants on healing of surgically created circumferential gap in dogs

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## 감사의 글

비록 작은 결실이지만 오늘이 있기까지 항상 부족한 저를 따뜻한 관심과 지도와 사랑으로 격려해주시고 이끌어주신 최성호 교수님께 깊은 감사를 드립니다. 그리고 항상 아버지처럼 따뜻하게 감싸주시고 인생과 학업에 있어서 많은 조언과 격려를 해주신 김종관 교수님께 감사드립니다. 또한 학교에 있을 때나 학교를 나와 세상을 살아가는 데에 있어 이끌어주신 채종규 교수님, 조규성 교수님, 김창성 교수님과 이 논문이 나오기까지 많은 가르침을 주신 이용근 교수님과 심준성 교수님, 그리고 담임반의 김형준 교수님께 진심으로 감사드립니다.

이 연구를 하는 동안 그리고 논문을 작성을 하는 동안 많은 도움을 아끼지 않았던 사랑하는 치주과 의국원 후배 여러분께 고마움을 전합니다.

학교에서 나와 넓은 세상으로 나왔을 때 그리고 이 논문이 나오기까지 많은 이해와 도움을 주신 임지순 원장님과 많은 선배님들께도 감사드립니다. 항상 저의 튼튼한 후원자가 되어주시고 뿌리가 되어주신, 끝이 없는 사랑을 주시는 아버지, 어머니, 장인, 장모님께 진심으로 감사드립니다. 동생 보경이와 한 가족이 되어준 준호에게도 사랑과 고마움을 전합니다. 그리고 지금의 제가 있기까지 저를 복 돌와 주고 헌신을 다 해준 나의 사랑하는 아내 정인이에게 다시 한번 감사하며 진정으로 사랑과 고마움을 담아 이 논문을 드립니다.

모든 분들께 진심으로 감사드립니다.

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## **ABSTRACT**

### **The effects of Hydroxyapatite nano-coating implants on healing of surgically created circumferential gap in dogs**

Laboratory animal studies and experiences with human implants suggested that Hydroxyapatite (HA) coated dental implants could induce a chemical bond with bone and achieve biological fixation. The aim of this study was to compare the healing response of various HA coated dental implants by IBAD placed in the surgically created circumferential gap in dogs

In Four mongrel dogs, all mandibular premolars and the first molar were extracted. After an 8-weeks healing period, six submerged type implants were placed and the circumferential cylindrical 2mm coronal defects around the implants were made surgically with a customized step drill. In two groups, bone graft was performed additionally. Groups were divided into six- anodized surface, anodized surface with 150nm HA and 430°C heat treatment, anodized surface with 300nm HA and 430°C heat treatment, anodized surface with 150nm HA without heat treatment, anodized surface with bone graft and anodized surface with 150nm HA, 430°C heat treatment and bone graft. The dogs were sacrificed following a 12 -weeks healing period. Specimens were analyzed histologically and histomorphometrically.



During the healing period, healing was uneventful and implants were well maintained. Histologic analysis of the implants demonstrated newly formed, compact, mature bone with nearby marrow space, but there were volumetric differences between groups. The bone-to-implant contact (BIC) for anodized surface with 150nm HA, 430°C heat treatment and bone graft showed the highest value and the anodized surface with HA and 430°C heat treatment was also higher than the other groups. Bone density showed similar results as the BIC.

In conclusion, nano scale HA coated dental implants appear to have significant effect on the development of new bone formation. And additional bone graft is an effective method in overcoming the gaps around the implants.

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**Key Words:** Hydroxyapatite, Dental implant, Implant surface, Gap

# **The effects of hydroxyapatite nano-coating implants on healing of surgically created circumferential gap in dogs**

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## **I. Introduction**

Dental implants are used to replace the missing tooth, and have been used for more than 50 years (Albrektsson 1986). Dental implant treatment has obtained general consent by most clinicians worldwide. Initial stability and osseointegration are most important factors for the success of implant treatment. The stability of an implant is determined by the mechanical properties of the implant-bone interface, and the osseointegration of the interface has been commonly evaluated by histomorphometric analysis (Johansson 1991). Many attempts have been made over the past years to improve bone anchorage of dental implants. Implants placed in non compromised conditions presented similar success rate irrespective of its own design and surface.

However, the placement of implant in compromised sites needs the better and the faster osseointegration. Several studies presented that occurrence of dehiscence defect or coronal defect after implant placement results in poor osseointegration and increase the probability of implant failure. Nowadays, many implant systems are available and each system uses several types of surface treatment, aiming for optimal bone-implant contact. Buser (1991, 1998) has shown that the existence of surface roughness increase bone-to-implant contact. The roughness seems to favor the migration of undifferentiated mesenchymal cells, which cover the implant surface initially and maximize new bone formation (Cochran 1994). Many types of surface treatment have been proposed for increasing implant roughness. These include acid etching of the pure titanium surface, application of titanium plasma spray, blasting with different substances, oxidizing the titanium surface, and incorporating hydroxyapatite (HA). Experimental studies using various rough surface implants demonstrated significantly higher removal torques, and a higher percentage of bone-implant contact (Buser 1991) when compared with smooth surface titanium implants.

HA coated dental implants have shown excellent bone-to-implant contact and clinical survival rate (McGlumphy 2003). HA is an osteoconductive and osteoinductive ceramic and acts as strong biological bonding material between implants and bone tissue. HA have good biocompatibility, which induces superficial topographic irregularities. Laboratory animal studies and experiences with human implants suggested that HA coated dental implants could induce a chemical bond to bone and achieve biological fixation. Thomas (1987) has shown an increase of new

bone formation in the initial stage of osseointegration with the development of osteophylic surface. But controversy still persists over the long-term clinical effectiveness of HA-coated dental implants, because some reports suggest that the HA coating may separate from the substructure, undergo dissolution in tissue fluids, and contribute to rapid breakdown around the implants (Biesbrock 1995, Hanisch 1997, Liao 1997). This failure may be due to the differences in chemical composition of the HA on the implant surface and the structural changes of the coating, which dependent on coating method. HA coating on the dental implant can be applied by numerous methods. This includes electrophoretic deposition, dip coating, hot isostatic pressing, flame spraying, plasma spraying, and pulsed laser deposition. The most commonly used plasma spraying methods have some problems, ie, chemical nonuniformity of the coating layer and degradation in the physiologic human fluid. Also low adhesion strength between metal and HA coating still remains a problem(McGlumphy 2003).

Recently, nano coating of HA to the currently used implants or application of growth factors such as BMP have been developed for successful and better osseointegration. Of the several coating methods, ion beam- assisted deposition (IBAD) being recently developed to resolve these problems, has shown the favorable result(Jeffcoat 2003). The aim of this study was to compare the healing response of various nano size HA coated dental implants by IBAD placed in the surgically created circumferential gap in dogs

## **II . Materials and methods**

### **1. Materials**

#### **1.1 Implant**

Twenty four anodized surface, screw-type implants, 3.4mm in diameter and 10.0mm in length (Implantium®, Dentium, Seoul, Korea) were used. The implants of experimental groups were coated with HA using ion-beam-assisted reposition (IBAD).

#### **1.2 Grafted material**

Synthetic bone grafted material (Osteon®, Dentium, Seoul, Korea) was used. It is made of 70% of Hydroxyapatite (HA) and 30% of  $\beta$ - Tricalcium phosphate (TCP).

#### **1.3 Animals**

Four male Mongrel dogs, 18 to 24 months old and weighing about 30 kg, were chosen. The animals had intact dentition and healthy periodontium. Animal selection, management, preparation and surgical protocol followed the routine procedure approved by the Animal Care and Use Committee, Yonsei Medical Center, Seoul, Korea.

## **2. Methods**

### **2.1 Experimental Design**

Groups were divided according to implant surface and defect treatment. Control group was placed with anodized surface implants. Experimental group 1 was placed with anodized surface with HA coating, 150nm thickness and 430°C heat treatment and experimental group 2 was placed with anodized surface with HA coating, 300nm and 430°C. Experimental group 3 was placed with anodized surface with coating of 150nm HA but no heat treatment. Experimental group 4 was placed with anodized surface but was applied with the bone graft materials. (Osteon®, Dentium, KOREA) and experimental group 5 was placed with anodized surface with HA coating, 150nm thickness and 430°C heat treatment and bone graft.

### **2.2 Surgical protocol**

Teeth were extracted under general anesthesia in sterile conditions in an operating room using Atropine 0.05 mg/kg SQ, xylazine (Rompun®, Bayer Korea, Seoul, Korea.) 2 mg/kg, and ketamine hydrochloride (Ketalar®, Yuhan Co., Seoul, Korea) of 10 mg/kg IV. Dogs were placed on a heating pad, intubated, administered 2 % enflurane, and monitored with an electrocardiogram. After disinfecting the surgical

sites, 2 % lidocane HCl with epinephrine 1:100,000 (Kwangmyung Pharm., Seoul, Korea) was administered by infiltration at the surgical sites. Crevicular incisions were made and all premolars (P1-P4) and the first molar (M1) were carefully extracted. Prior to extraction, P2-P4 and M1 were sectioned to avoid tooth fracture. Flaps were sutured with 5-0 resorbable suture material (Polyglactin 910, braided absorbable suture, Ethicon, Johnson & Johnson Int., Edinburgh, U.K.) by the vertical mattress suture technique. On the day of the surgery, the dogs received 10 mg/kg IV of the antibiotic Cefradin (Cefradin<sup>®</sup>, Choongwae Pharm, Seoul, Korea)

The implants (Implantium<sup>®</sup>, Dentium, Seoul, Korea) were placed after 8 weeks of healing period using the same surgical conditions as those for tooth extraction. A crestal incision was made to preserve keratinized tissue, and mucoperiosteal flaps were carefully reflected on the buccal and lingual aspects. The edentulous ridge was carefully flattened with a ridge contouring bur and irrigated with sterile saline. Three submerged type implants (3.4 mm diameter, 10.0 mm length) were placed on each side of the mandible. Implant osteotomy was performed at 800 rpm under chilled saline irrigation. And circumferential defects of 2.0 mm gaps were created surgically with a customized paralleled step drill. Implant placement was made without tapping to obtain good initial stability. In two groups (anodized surface implant, anodized surface coated 150nm HA with 430°C heat treatment), additional bone graft (Osteon<sup>®</sup>, Dentium, Seoul, Korea) was performed around the fixtures (Figure 1, 2). Flaps were closed with a 5-0 resorbable suture material and implants were submerged. Post-

operative care was similar as that for tooth extraction. Sutures were removed after 7 to 10 days and a soft diet was provided throughout the study period.

Dogs were sacrificed at 12 weeks after surgery. Euthanasia was performed by anesthesia drug overdose. Block sections including segments with implants were preserved and fixed in 10 % neutral buffered formalin.

## **2.3 Evaluation Methods**

### **2.3.1 Clinical evaluation**

### **2.3.2 Histologic analysis**

The specimens were dehydrated in ethanol, embedded in methacrylate, and sectioned in the mesio-distal plane using a diamond saw (Exakt®, Apparatebau, Norderstedt, Germany). From each implant site, the central section was reduced to a final thickness of about 20  $\mu\text{m}$  by microgrinding and polishing with a cutting-grinding device, Exakt®. The sections were stained in hematoxiline-eosine.

General histological findings were observed with a stereoscope (LEICA MZFLIII, LEICA, WETZLAR, Germany) and light microscope.

### **2.3.3 Histometric analysis**

After conventional microscopic examinations, computer-assisted histometric measurements were obtained using an automated image analysis system (Image-Pro



Plus<sup>®</sup>, Media Cybernetics, Silver Spring, M.D.) coupled with a video camera mounted on a light microscope (LEICA DM-LB, LEICA, WETZLAR, Germany).

The measuring parameter were as follows.

- 1) Bone to implant contact percentage (BIC %) in the coronal 5mm of the implant
- 2) Newly formed bone density within the threads in the coronal 5mm of the implant

#### **2.3.4 Statistical Analysis**

The means and the standard deviation for each of the 6 groups were calculated. The significance of the difference for the groups was determined by the Kruskal-Wallis test ( $P < 0.05$ ).

### **III. Results**

#### **1. Clinical findings**

During the postoperative period, healing was uneventful and implants were well-maintained. There were no signs of inflammation observed in the mucosa adjacent to the implants.

#### **2. Histologic analysis**

Histologic analysis of the implants demonstrated newly formed, compact, mature bone with nearby marrow space, but there were volumetric differences between groups (Figure 3- 8). In the control –anodized surface group, most of the coronal gaps were not filled with bone, and minimal new bone formation was shown (Figure 3). Coronal gaps were filled with loose connective tissues, and some epithelial apical migration was observed. The microthread portion of the implant in the control groups did not show osseointegration.

The Experimental group 1, 2 -anodized surface with HA coating and 430°C heat treatment showed an improved regenerative characteristics(Figure 4, 5). Most of the gaps were filled with newly regenerated bone. The implant surface was covered with

a bone layer as a base for intensive bone formation and remodeling. The implant surface were lined with osteoblasts and showed a favorable contact osteogenesis. Especially experimental group 1- 150nm coating and 430 °C heat treatment- showed more favorable bone formation. Most of the newly formed bone was compact and mature. The coronal microthreads portion showed no connective tissue invagination and epithelial migration (Figure 4). In experimental group 2- 300nm coating and 430 °C heat treatment, there was also good bone filling around the implant surface, but there were some bony resorption in the coronal microthread portion (Figure 5). The two or three microthread of the most coronal part did not show bone fill and osseointegration, but the other part of the implant was lined with newly formed bone just same as the experimental group 1.

Experimental group 3 - anodized surface with 150nm HA coating and no heat treatment-showed minimal bone fill and less osteointegration as that of the control (Figure 6). There was connective tissue invasion and bony resorption in the coronal microthread.

When grafting the alloplastic material to the gaps- experimental group 4, 5, most of the coronal gaps were filled with newly formed bone and the remaining graft particles (Figure 7, 8). The newly formed bone was observed above the implant top and favorable bone to implant contact was also seen. Grafted bone particles still remained and was not resorbed yet. The remaining particles were surrounded by the new bone. Newly formed bone trabeculae were present, which were composed

mostly of the woven bone. The new bone was in direct apposition to the HA particles and implant titanium surface.

### **3. Histometric analysis**

The results from the histometric analysis is presented in Table 1, 2.

The BIC and bone density parameters showed similar results with the histological findings. The bone graft group presented the best BIC value which had statistical significance. Experimental group 1 presented the highest mean value in bone density, which was statistically significant. The anodized surface with HA coatings and 430 °C heat treatment showed favorable results in terms of BIC and the bone density compared to the control and no heat treatment groups. But there was no statistical significance between those groups.

**Table 1. Bone to Implant Contact (BIC) (n=4)**

	Mean±SD
Control (Anodized surface)	0.288±0.099
Experimental 1(Anodized HA150nm, 430 °C)	0.496±0.112
Experimental 2(Anodized HA 300nm, 430 °C)	0.368±0.108
Experimental 3(Anodized HA 150nm, no heat)	0.276±0.106
Experimental 4 (Anodized+ Bone graft)	0.571±0.116 <sup>†</sup>
Experimental 5 (Anodized HA 150nm, 430 °C +bone graft)	0.505±0.121 <sup>†</sup>

SD: standard deviation

<sup>†</sup> statistical significance p<0.05

**Table 2. Bone density (n=4)**

	Mean±SD
Control (Anodized)	0.338±0.124
Experimental 1(Anodized HA150nm, 430 °C)	0.599±0.116 <sup>†</sup>
Experimental 2(Anodized HA 300nm, 430 °C)	0.431±0.129
Experimental 3(Anodized HA 150nm, no heat)	0.306±0.152
Experimental 4 (Anodized+ Bone graft)	0.531±0.118
Experimental 5 (Anodized HA 150nm, 430 °C +bone graft)	0.475±0.135

<sup>†</sup> statistical significance p<0.05

## **IV. Discussion**

In the late 1950s, Brånemark predictably achieved an intimate bone-to-implant apposition that offered sufficient strength to cope with load transfer. This phenomenon is called “osseointegration” and after that a series of screw-shaped, commercially pure titanium implants were inserted in the edentulous area. Since that time, millions of patients have been treated worldwide using dental implant, and now, dental implant treatment has obtained general consent by most of the clinicians. A key element in the reaction of hard and soft tissues to an implant involves the implant's surface characteristics- the chemical and physical properties. Implants placed in non compromised bone quality and quantity presented similar implant success rate irrespective of implant surface treatments(Kim 2007). However, increase in implant placement specially in compromised sites with previous periodontitis, sinus pneumatization, poor bone quality or in cases where immediate implant placement is required increases the need for a better and a faster osseointegration. Several studies presented that occurrence of dehiscence defect or coronal defect after implant placement results in poor osseointegration and increase the risk of implant failure(Cho 1998, Jung 2005, Kim 2006). In such situations, additional bone graft procedure or a use of a membrane is required for better implant success.

In the early years of implant placement, machined type implants with pure titanium surfaces was used. However, since several studies presented the advantage of rough

surface for successful osseointegration, many researches on developing a favorable implant surface were performed until today. It is generally believed that the rough surfaces accelerate the initial healing phase and enhance bone formation at the implant surface(Buser 1998, Ericsson 1994, Klokkevold 1997). Roughening the topography of the implant surface by applying a porous coating or through surface treatments may promote osteogenesis by enhancing osteoblast metabolic activity and cellular adhesion, increasing surface area, and stabilizing the fibrin scaffold. Thus faster bone apposition can be achieved with roughened surfaces compared to machined surfaces(Wong 1995). The chemical nature of the implant surface can be modified by coating its surface. Some materials, as well as various surface characteristics, enhance bone apposition at the implant surface in an osteoconductive manner.

Calcium phosphate, especially hydroxyapatite (HA,  $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$ ) have been a popular coating material because of its resemblance to bone tissue. HA is an osteoconductive and osteoinductive ceramic and promotes strong biological bonding between implants and bone tissue. Although long-term clinical studies have presented highly successful results for HA-coated implants(Block 1996, McGlumphy 2003, Thomas 1987), some researchers have expressed concerns about the potential for dissolution, resorption, and detachment of the coating, which may promote the loss of osseointegration(Biesbrock 1995, Hanisch 1997, Liao 1997). Usually this may be due to the macroscopically visible surface roughness. Macroscopically rough surfaces have the tendency of progressive bone loss, susceptibility to the contamination of oral

bacteria and leading ultimately to implant loss. The 2<sup>nd</sup> generation implants with HA coating or acid etched surface enhanced implant surface roughness but have presented limitations and complications. The 3<sup>rd</sup> generation implants with SLA, anodizing, and RBM surfaces are currently mainly used. However, in order to achieve a faster and a superior osseointegration, studies on nano coating or application of growth factors such as BMP to the currently used implants are being carried out.

In the present study, nano scaled HA coated implant were used. Basically the implant which were used had an anodized surface. This surface used titanium oxide(TiO<sub>2</sub>) layers to enhance or accelerate the bone formation. In our study, we hypothesized that combining the anodized surface and HA deposition would have synergistic effect. In the present study, we used 150nm or 300nm thickness HA coated implants to evaluate the effects of HA coatings on the anodized surface of endosseous dental implants whether osseointegration of implants with such HA coating occurs earlier. In analyzing the results of the histologic and histometric analysis, HA coated dental implant showed favorable results compared to the control anodized surface implant. Anodized surface implant group showed minimal bone fill of the surgically created gaps and low BIC and bone density value. The HA coated implant groups presented almost double sized value in BIC and bone density and the gaps were almost filled with newly regenerated bone. Especially 150nm HA coated implant showed more favorable results than 300nm coated implant. In bone density parameter, 150nm HA coated implant group showed statistically different value compared to 300nm coated implant group. In anodized implant, there are its own micropores on



their surface and their average roughness is about  $0.37\mu\text{m}$ . When very thick layer of HA is coated on the anodized implant, the micropores are blocked by HA particles (Sul 2005). Our results may be due to these characteristics of oxidized implant. And HA must be resorbed according to the bone healing time and must be replaced with bone. However, it is unfavorable for the bone to be replaced and takes more time to melt as the layer gets thick.

In terms of heat treatment, we compared the same thickness HA coated implant with or without of  $430^{\circ}\text{C}$  heat treatment. Oonishi(1999) suggested that the amorphous phase of the coatings, which has a greater resorption in vivo than crystalline HA coating, can accelerate the early fixation of the implant with bony tissue and promote fast bone remodeling and attachment. However, it is also known that a high concentration of amorphous phase in the coating can cause excessive dissolution, consequently reduce the coating integrity of the implants. In addition in vitro and vivo research also suggested that the crystallinity of HA coatings is essential to their biocompatibility and early performance when compared to machined implants (Ong 2002, Brugge 2002). In our results, anodized surface with HA coating and no heat treatment showed minimal bone fill and less osseointegration as that of the control group. The reason for this being is that there is a fast melting characteristic with amorphous HA layer when there is no heat treatment, in consequent, there is an unfavorable effect in terms of osseointegration and there happens to be a gap between the implant surface and the bone surface.

In the present study, circumferential parallel 2mm defect was created surgically. The surgically created 2mm circumferential defect used in the present study is a critical sized defect where complete bone filling does not occur naturally. The defect reproduces coronal gaps occurring during clinical practices and was used to compare the degree of osseointegration on implant surfaces. Several studies suggested that gaps larger than 2mm resulted in a smaller amount of direct bone to implant contact (Akimoto 1999, Knox 1991, Jung 2007). Clinically many methods have been introduced to overcome the coronal gap associated with immediate implant (Becker 1994, Lang 1994, Werbitt 1992). Additionally, in this study, Bone particle was grafted into the surgically created gaps for evaluating the synergistic effects of bone materials and HA surface of implants. Bone material (Osteon<sup>®</sup>) is the mixture of HA and beta-tricalcium phosphate ( $\beta$ -TCP). HA provides a good scaffold for the new bone to growth, but has poor regeneration potential.  $\beta$ -TCP has good bone regeneration potential, but is not able to provide sufficient space for bone growth. Mixing HA and  $\beta$ -TCP permits the association between the physico-chemical properties of each compound. Recent studies have suggested the stability and effectiveness of the mixture of HA and  $\beta$ -TCP (Cornell 1995, Schopper 2005). The present study showed the superior results in histologic and histometric analysis. Most of the gap areas were filled with newly formed bone. In some histologic view, we can see that the new bone was formed above the implant top. In BIC and bone density parameters, it also showed favorable values compared to the other groups.

The object of this study was to evaluate the effects of nano size HA coating to the

anodized surface of dental implant, and the synergistic effects of bone graft. In our study, the thin coating of HA to the implant surface enhances the osseointegration even in the surgically created gaps. And additional bone graft synergistically promotes the new bone formation in HA coated dental implants.

Even if more researchs are necessary on the long term effects of HA coated implants, in conclusion, HA coated dental implants appears to have significant effects on the development of new bone formation.

## **V. Conclusion**

In conclusion, nano scale HA coated dental implants appear to have significant effect on the development of new bone formation. And additional bone graft is an effective method in overcoming the gaps around the implants.

## VI. Reference

Akimoto, K., Becker, W., Persson, R., Baker, D.A., Rohrer, M.D., O'Neill, J.C. (1999) Evaluation of titanium implants placed into simulated extraction socket: A study in dogs. *International Journal of Oral & Maxillofacial Implants* 13:351-360

Albrektsson, T., Jansson, T., Lekholm, U. (1986) Osseointegrated dental implants. *Dental Clinics of North America* 30:151-174

Becker, W., Dahlin, C., Becker, B.E., Lekholm, U., Van Steenberghe, D., Higuchi-Kultje, C. (1994) The use of e-PTFE barrier membranes for bone promotion around titanium implants placed into extraction sockets: A prospective multicenter study. *International Journal of Oral & maxillofacial Implants* 9:31-40

Biesbrock, A.R., Edgerton, M. (1995) Evaluation of the clinical predictability of hydroxyapatite-coated endosseous dental implants: A review of the literature. *International Journal of Oral & Maxillofacial Implants* 10:712-720

Block, M.S., Kent, J.N. (1996) Long term follow up on hydroxyapatite coated cylindrical dental implants: A comparison between development and recent periods. *International Journal of Oral & Maxillofacial Implants* 11:626-633

Brugge, P.J., Jansen, J.A. (2002) Initial interaction of rat bone marrow cells with non-coated and calcium phosphate coated titanium substrates. *Biomaterials* 23:3269-3277

Buser, D., Schenk, R.K, Steinemann, S., Fiorellini, J.P., Fox, C.H., Stich, H. (1991) Influence of surface characteristics on bone integration of titanium implants. A histomorphometric study in miniature pigs. *Journal of Biomedical Material Research* 25:889-902

Buser, D., Nydegger, T., Hirt, H.P., Cochran, D.L., Nolte, L.P. (1998) Removal torque values of titanium implants in the maxilla of miniature pigs. *International Journal of Oral & Maxillofacial Implants* 13:611-619

Cho, K.S., Choi, S.H., Han, K.H., Chao, J.K., Wikesjö ,U.M.E., Kim, C.K. (1998) Alveolar bone formation at dental implant dehiscence defects following guided bone regeneration and xenogenic freeze-dried demineralized bone matrix. *Clinical Oral Implant Research* 9:419-428

Cochran, D.L., Simpson, J., Weber, H.P., Buser D. (1994) Attachment and growth of periodontal cells on smooth and rough titanium. *International Journal of Oral & Maxillofacial Implants* 9:289-297

Cornell, C.N., Lane, J.M. (1998) Current understanding of osteoconduction in bone

regeneration. *Clinical Orthopaedics and Related Research* 355 Suppl:S267-273.

Ericsson, J., Johansson, C. B., Bystedt, H. (1994) A histomorphometric evaluation of bone-to-implant contact on machine-prepared and roughened titanium dental implants: a pilot study in dog. *Clinical Oral Implant Research* 5:202-206

Hanisch, O., Cortella, C.A., Boskovic, M.M., James, R.A., Slots, J., Wikesjö, U.M. (1997) Experimental peri-implant tissue breakdown around hydroxyapatite-coated implants. *Journal of Periodontology* 68:59-66

Jeffcoat, M.K., McGlumphy, E.A., Reddt, M.S., Geurs, N.C., Proskin, H.M. (2003) A comparison of hydroxyapatite (HA)-coated threaded, HA-coated cylindrical, and titanium threaded endosseous dental implant. *International Journal of Oral & Maxillofacial Implants* 18:406-410

Johansson, C.B., Albrektsson, T. (1991) A removal torque and histomorphometric study of commercially pure niobium and titanium implants in rabbit bone. *Clinical Oral Implants Research* 2:24-29

Jung, U.W., Kim, C.S., Choi, S.H., Cho, K.S., Inoue, T., Kim, C.K. (2007) Healing of surgically created circumferential gap around non-submerged-type implants in dogs: a histomorphometric study. *Clinical Oral Implants Research* 18:171-178

Jung, U.W., Moon, H.I., Kim, C.S., Lee, Y.K., Kim, C.K., Choi, S.H. (2005) Evaluation of different grafting materials in three-wall intrabony defects around dental implants in beagle dogs. *Current Applied Physics* 5:507-511

Kim, M.K., Choi, J.Y., Jung, U.W., Lee, I.S., Inoue, T., Choi, S.H. (2007) The Effects of ion beam-assisted deposition of Hydroxyapatite on the osseointegration of endosseous implant surface. *Key Engineering Materials* 330-332: 597-600

Kim, Y.S., Kim, T.G., Jung, U.W., Kim, C.S., Choi, S.H., Cho, K.S., Kim, C.K. (2006) Histomorphology on healing of the chitosan membrane and  $\beta$ -TCP on dental implant dehiscence defects in dogs. *Key Engineering Materials* 309-311: 255-258

Klokkevold, P., Nishimura, T., Adachi, M. (1997) Osseointegration enhanced by chemical etching of the titanium surface. *Clinical Oral Implant Research* 8:442-447

Knox, R., Caudill, R., Meffert, R. (1991) Histologic evaluation of dental endosseous implants placed in surgically created extraction defects. *International Journal of Periodontics and Restorative Dentistry* 11:364-375

Lang, N., Bragger, U., Hammerle, C., Sutter, F. (1994) Immediate transmucosal implants using the principle of guided tissue regeneration: Rational, clinical



procedures and 30-month results. *Clinical Oral Implants Research* 5:154-163

Liao,H., Fartash,B., Li, J. (1997) Stability of hydroxyapatite-coatings on titanium oral implants(IMZ).2 retrieved cases. *Clinical Oral Implants Research* 8:68-72

McGlumphy, E.A., Peterson, L.J., Larsen, P.E., Jeffcoat. M.K. (2003) Prospective study of 429 hydroxyapatite-coated Cylindric Omniloc Implants placed in 121 patients. *International Journal of Oral & Maxillofacial Implants* 18:82-92

Oonishi, H., Hench, L.L., Wilson, J., Sugihara, F., Tsuji, E., Kushitani, S., Iwaki, H. (1999) Comparative bone growth behavior in granules of bioceramic materials of various sizes. *Journal of Biomedical Material Research* 44:31-43

Ong, J.L., Bassho, K., Cavin, R., Carnes, D.L. (2002) Bone response to plasma-sprayed hydroxyapatite and radiofrequency-sputtered calcium phosphate implants in vivo. *International Journal of Oral & Maxillofacical Implants* 17:581-586

Schopper, C., Ziya-Ghazvini, F., Goriwoda, W., Moser, D., Wanschitz, F., Spassova, E., Lagogiannis, G., Auterith, A., Ewers, R.(2005) HA/TCP compounding of a porous CaP biomaterial improves bone formation and scaffold degradation--a long-term histological study. *Journal of Biomedical Material Research B. Applied Biomaterials* 74:458-467.

Sul, Y.T., Johansson, C., Wennerberg, A., Cho, L.R., Chang, B.S., Albrektsson, T. (2005) Optimum surface properties of oxidized implants for reinforcement of osseointegration: Surface chemistry, oxide thickness, porosity, roughness, and crystal structure. *International Journal of Oral & Maxillofacial Implants* 20:349-359

Thomas, K.A., Kay, J.F., Cook, S.D., Jarcho, M. (1987) The effect of surface macrotexture and hydroxyapatite coating on the mechanical strengths and histologic profiles of titanium implant materials. *Journal of Biomedical Material Research* 21:1395-1414

Werbitt, M., Goldberg, P. (1992) The immediate implant: Bone preservation and bone regeneration. *International Journal of Periodontics and Restorative Dentistry* 12:206-217

Wong, M., Eulenberger, J., Schenk, R., Hunziker, E. (1995) Effect of surface topography in the osseointegration of implant materials in trabecular bone. *Journal of Biomedical Material Research* 29:1567-1576

## Figure legends

Figure 1. Clinical photpgraph representing the experiment. 2.0mm gaps were prepared and bone material was grafted

Figure 2. Radiographic view of the experimental site. 10mm implant was implanted

Figure 3. Histologic view of control group. (Anodized surface implant) A: maginification x 10, B: x 100

Figure 4. Histologic view of experimental group 1. {Anodized surface implant + Bone (Osteon<sup>®</sup>: HA+ TCP) graft} A: maginification x 10, B: x 100

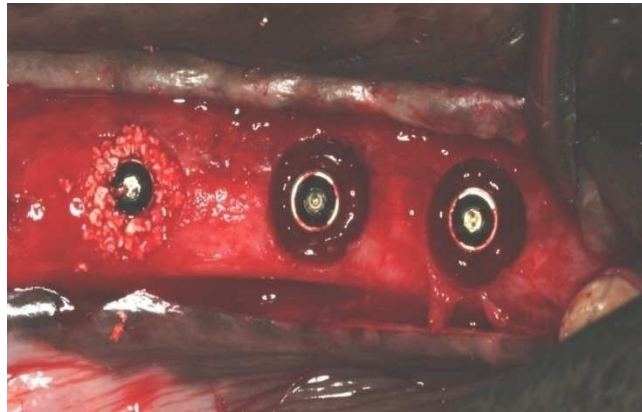
Figure 5. Histologic view of experimental group 2. (Anodized surface + HA 150nm coating +430°C heat treatment implant) A: maginification x 10, B: x 100

Figure 6. Histologic view of experimental group 3. (Anodized surface + HA 300nm coating +430°C heat treatment implant) A: maginification x 10, B: x 100

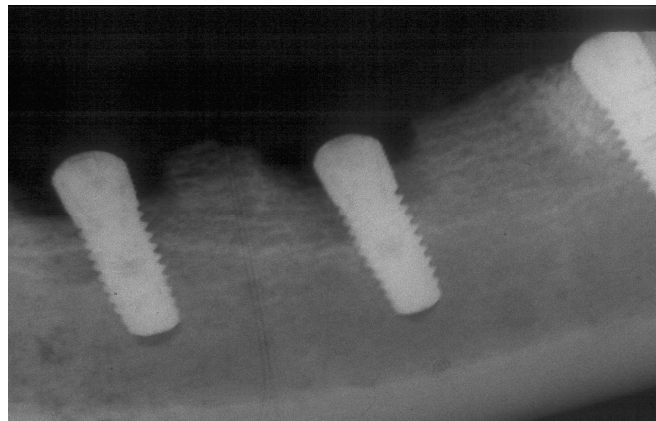
Figure 7. Histologic view of experimental group 4. (Anodized surface + HA 150nm coating no heat treatment implant) A: maginification x 10, B: x 100

Figure 8. Histologic view of experimental group 5. {Anodized surface + HA 150nm coating +430°C heat treatment implant + Bone(Osteon<sup>®</sup>: HA+ TCP) graft} A: maginification x 10, B: x 100

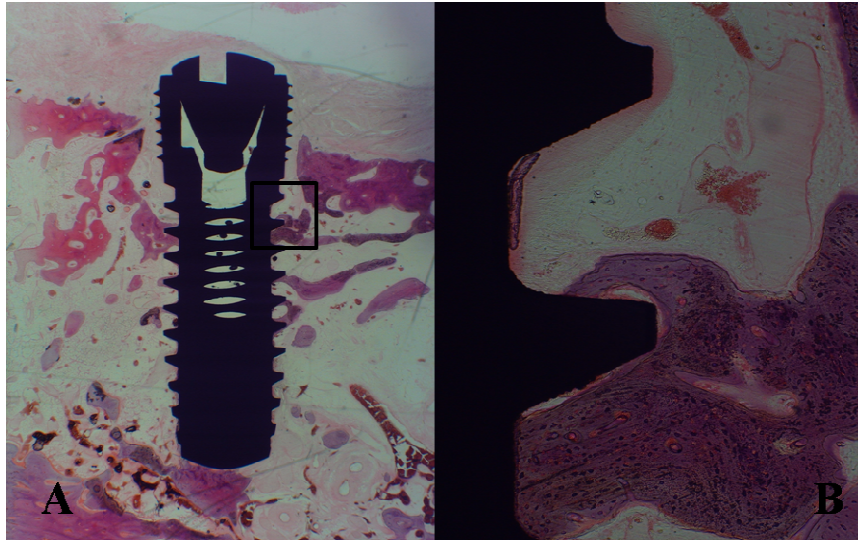
## Figures



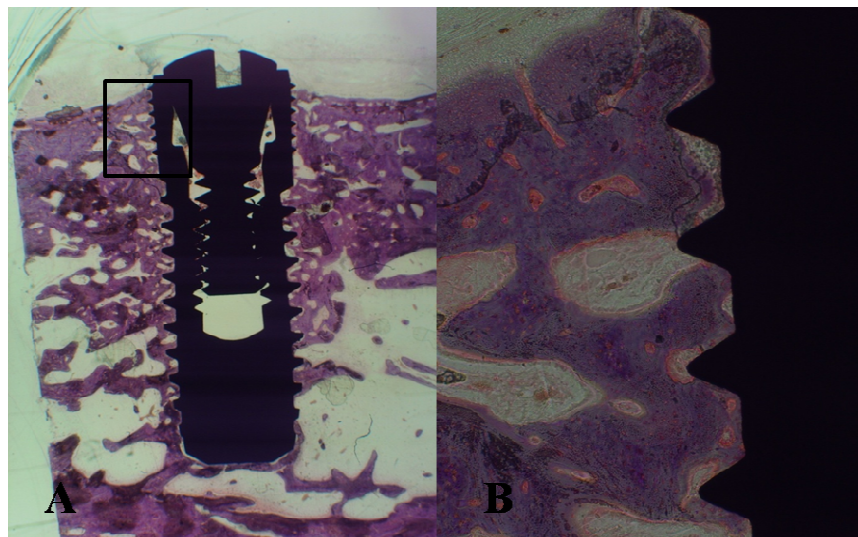
**Figure 1**



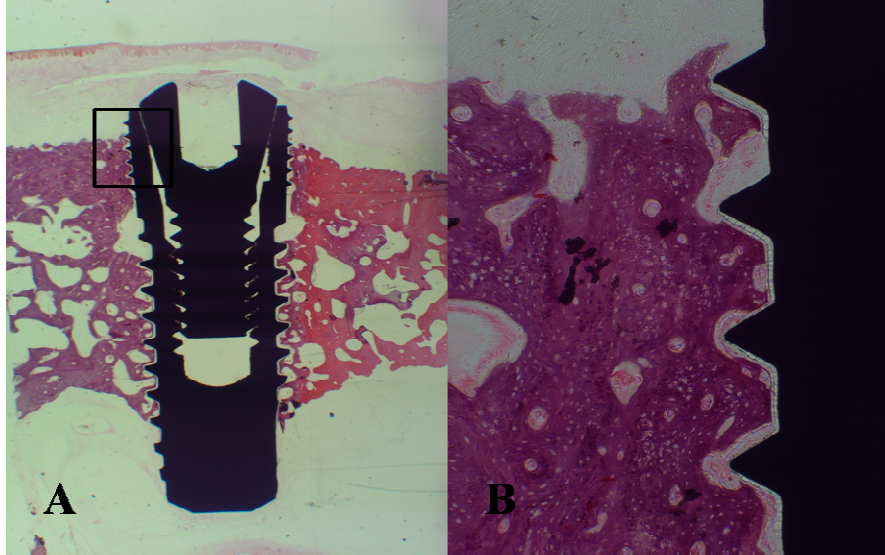
**Figure 2**



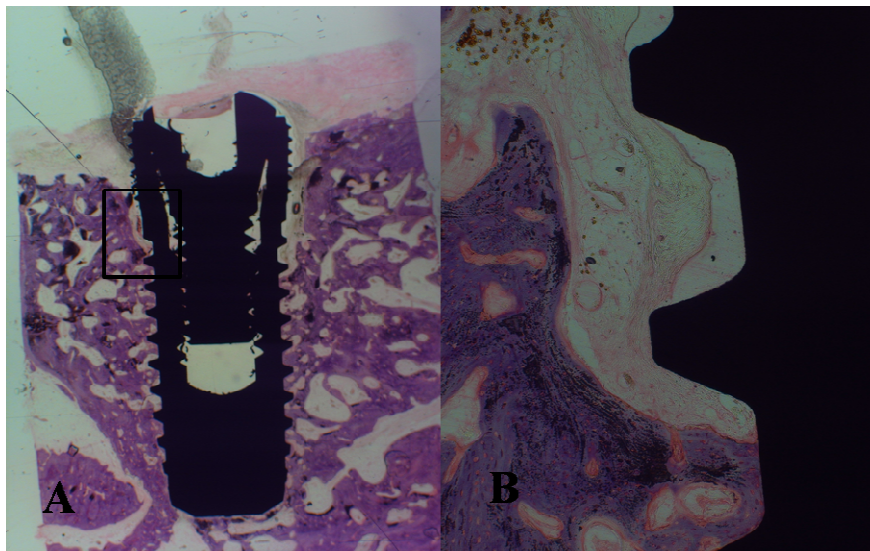
**Figure 3**



**Figure 4**

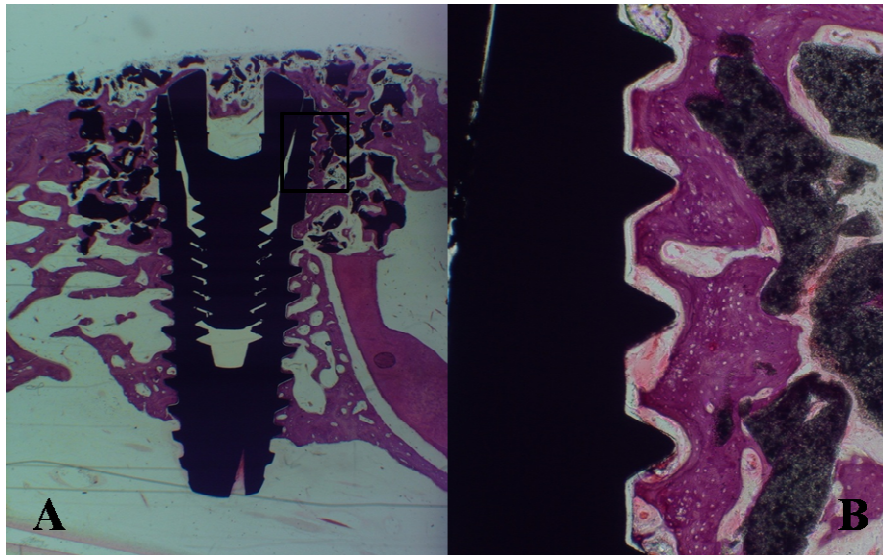


**Figure 5**



**Figure 6**





**Figure 7**



**Figure 8**

## 국문요약

# 성견에서 하이드록시 아파타이트 나노 코팅 임플란트가 외과적으로 형성한 환상형 결손부의 치유에 미치는 영향

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<지도 최성호 교수>

채 경 준

많은 연구들에서 하이드록시아파타이트 코팅 임플란트가 골과 화학적 결합을 일으키며 골유착에 있어서 우수한 결과를 나타낸다고 보고되어져왔다. 이 실험의 목적은 하이드록시아파타이트를 나노코팅한 임플란트가 성견에서 외과적으로 형성한 골 결손부의 치유에 있어 어떤 영향을 미치는지 알아보고자 하였다.

총 네마리의 수컷 잡견에서, 모든 하악 소구치와 제일 대구치를 발거하고 8주동안 치유시킨 후 각 6개씩의 매몰형 임플란트를 식립하였다. 임플란트 부위에 주문 제작한 평행형 드릴을 이용하여 치관부에 환상형 골 결손부를 형성하였으며 두 군에서는 부가적으로 골이식을 시행하였다. 대조군으로는 아노다이징 표면, 실험군은 임플란트의 표면처리에 따라, 아노다이징 표면에 150nm의 하이드록시아파타이트를 코팅한 후 430°C 열처리,



아노다이징 표면에 300nm 하이드록시아파타이트 코팅 및 열처리, 아노다이징 표면에 150nm 하이드록시아파타이트 코팅, 아노다이징 표면에 골이식, 그리고 아노다이징 표면에 150nm의 하이드록시아파타이트를 코팅한 후 430°C 열처리, 골이식으로 나누었다. 12주간의 치유기간 후에 희생하여 조직절편을 얻었으며 이를 조직학적 및 조직계측학적으로 관찰하였다.

치유기간동안 임플란트는 잘 유지되었다. 조직학적 관찰결과 임플란트 주변 결손부로 새로이 형성된 골조직이 나타났으며 군간에 골양에 있어 차이를 나타내었다. 골과 임플란트의 골유착정도에 있어서 아노다이징 표면에 150nm의 하이드록시아파타이트 코팅 후 열처리한 임플란트에 부가적으로 골이식을 한 군이 가장 우수하였으며, 하이드록시아파타이트 코팅 후 열처리한 실험군에서는 골이식을 하지 않더라도 대조군에 비해 우수한 골유착 정도를 나타내었다. 골밀도에 있어서도 골유착 정도와 유사한 결과를 나타내었다.

결론적으로 하이드록시아파타이트 나노 코팅 임플란트는 신생골 형성에 있어서 유리한 영향을 미치며, 임상적으로 부가적인 골이식은 임플란트 주위 결손부의 치유에 있어 유용한 치료방법이다.

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**핵심되는 말:** 하이드록시아파타이트, 치과용 임플란트, 임플란트 표면, 결손부